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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,651	01/22/2005	Oleg Iliich Epshtein	841/007	7491

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EXAMINER	
PAK, MICHAEL D	
ART UNIT	PAPER NUMBER
1646	
MAIL DATE	DELIVERY MODE
10/07/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,651	EPSHTEIN ET AL.	
	Examiner	Art Unit	
	Michael Pak	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3 and 5-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3 and 5-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8-16-10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Amendment filed July 7, 2010 has been entered. Claims 3 and 5-10 are pending. Claims 1-2, 4 are cancelled.

2. Applicant's arguments filed July 7, 2010, have been fully considered but they are not found persuasive.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 3 and 5-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims recite or encompass the term “homeopathically potentized form” which is ambiguous and confusing because the metes and bounds of the term is not clear. It is not clear when a compound is homeopathically potentized form because it does not appear to be different from the cited reference forms.

Applicants argue that the Declaration of . Oleg I Epstein and Vasilij Nikolayevich Nikolayev under 37 CFR 1.132 provides evidence that one skilled in the art are aware of the term. However, the it is not clear where the metes and bounds of when a material is a homeopathically potentized form or at such low dilution where there are no products present. It is not clear to all skilled in the art that such form is clear. Goldacre (Lancet, 2007) disclose that homeopathy produced no statistically significant benefit over placebo. The state of the art is such that it is not clear what the product is that is giving the placebo effect.

Applicants argue that the evidence presented by the examiner is not relevant to the indefiniteness inquiry because the none of the studies reviewed or discussed in the Lancet article describes antibodies and the claimed invention relates to "homeopathically potentized form" of antibodies. However, the Goldacre disclose that similar methods of dilutions results in activity of homeopathic products which are not statistically significant over the placebo. Thus the metes and bounds of the claims are not clear because it is not clear when such homeopathic methods are used what is the product which is acting on the placebo effect that is being claimed. The metes and bounds of the product being claimed is not clear.

Applicants argue that the evidence in the file wrapper establishes that the claimed "homeopathically potentized" form of antibodies has activity. However, Goldacre teaches that effects of homeopathic products have activity which is not statistically significant over the placebo effect.

Applicants argue that the claims have been amended to define the term "homeopathically potentized form of … antibody …" and the claim language makes clear the genesis of the claimed "homeopathically potentized form" of antibody. However, the methodology of multiple dilutions does not make clear what the metes and bounds of the product is being claimed because the applicant has not defined what the product is when the product is in "homeopathically potentized form."

4. Claims 3 and 5-10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims encompass an antibody which is homeopathically potentized form. However, the essential feature of the invention is not clear because the structure which makes an antibody homeopathically potentized is not disclosed. Using the disclosure one of skilled in the art cannot envision the homeopathically potentized molecules of the claimed antibody molecules for the treatment. The claims encompass a form or structure which cannot be described in the specification. The antibody is diluted and becomes homeopathically potentized. The genus of molecules which is homeopathically potentized is not clear. *University of California v. Eli Lilly and Co. (CAFC) 43 USPQ2d 1398* held that a generic claim to human or mammalian when only the rat protein sequence was disclosed did not have written description in the

specification. If one skilled in the art cannot envision the generic claim from the specific example then it lacks written description. Homeopathically potentized antibody cannot be envisioned by one skilled in the art. The declarations present opinions of one skilled in the art of homeopathy that the specification discloses homeopathic potentized antibody. However, the state of the art is such that there appears to be a division between the homeopathy artisan and non-homeopathy artisans. Goldacre (Lancet, 2007) disclose that homeopathy produced no statistically significant benefit over placebo. The state of the art is such that one cannot envision what the product is that is giving the placebo effect.

Applicants argue that specification description is sufficient to establish possession and declaration and the references in the art describe the methodology of homeopathically potentized form. However, the methodology does not appear to disclose the claimed "homeopathically potentized form". The nexus between the method of making the product and resulting product which is“”homeopathically potentized form” is not disclosed in a manner that one of skilled in the art can determine what is the product claimed. Goldacre (Lancet, 2007) disclose that homeopathy produced no statistically significant benefit over placebo. The state of the art is such that one skilled in the art cannot reproduce the "homeopathically potentized form" with an activity which is not a placebo effect. The disclosure of the specification does not provide a nexus between the method of making the product and resulting product which is“”homeopathically potentized form” in a manner such that one of skilled in the art can determine what is the product claimed.

Applicants argue that a skilled artisan would make multiple consecutive dilutions until the antibody is potentized and show activity in an accepted model of pharmacological activity. However, Goldacre reference clearly shows that one skilled in the art cannot make multiple consecutive dilutions and create a potentized product and cannot show in an accepted model an activity that is more than a placebo effect.

5. Claims 3 and 5-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the antibody such as those disclosed in Le et al., does not reasonably provide enablement for a homeopathically potentized form of antibody. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The first paragraph of § 112 requires that the patent specification enable "those skilled in the art how to make and use the full scope of the claimed invention without `undue experimentation.'" Genentech, Inc. v. Novo Nordisk AIS, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)); see also In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). ("[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art."). Whether making and using the invention would have required undue experimentation, and thus whether the disclosure is enabling is a legal conclusion based upon several underlying factual inquiries. See In re Wands, 858 F.2d

731, 735, 736-37, 8 USPQ2d 1400, 1402, 1404 (Fed. Cir. 1988). As set forth in Wands, the factors to be considered in determining whether a claimed invention is enabled throughout its scope without undue experimentation include the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims.

Likewise, in Amgen Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991), the court affirmed the holding of invalidity of claims to analogs of the EPO gene under § 112 for lack of enablement where applicants had claimed every possible analog of the EPO gene but had disclosed only how to make EPO and a very few analogs. "[D]espite extensive statements in the specification concerning all analogs of the EPO gene that can be made, there is little enabling disclosure of the particular analogs and how to make them .... There may be many other genetic sequences that code for EPO-type products. Amgen has told how to make and use only a few of them and is therefore not entitled to claim all of them." Id., 927 F.2d at 1213-14, 18 USPQ2d at 1027.

Claims encompass a a homeopathically potentized form of antibody However, one skilled in the art cannot make and use homeopathically potentized form of antibody for treatment. The state of the art is such that one skilled in the art prior to the time of the invention found that homeopathically potentized form are no better than placebo (Goldacre (Lancet, 2007)). Goldacre (Lancet, 2007) disclose that homeopathy

produced no statistically significant benefit over placebo. The amount of direction provided in the specification is limited to diluting TNF antibodies. One skilled in the art cannot discern where the product is produced which results in a treatment which is different from placebo. One skilled in the art would require empirical experimentation in order to determine the difference between placebo effect and the treatment due to the potentized homeopathically form. In view of the extent and the unpredictability of the experimentation required to practice the invention as claimed, one skilled in the art could not make the invention without undue experimentation.

Therefore, based on the above Wands analysis, a preponderance of the evidence supports a conclusion that one skilled in the art would not have been enabled to make and use the claimed invention without undue experimentation.

Applicants argue that a skilled artisan would make multiple consecutive dilutions until the antibody is potentized and show activity in an accepted model of pharmacological activity. However, one skilled art cannot make and use a "homeopathically potentized form" of a product. The state of the art is such that one skilled in the art prior to the time of the invention found that homeopathically potentized form are no better than placebo (Goldacre (Lancet, 2007)). Goldacre (Lancet, 2007) disclose that homeopathy produced no statistically significant benefit over placebo. The amount of direction provided in the specification is limited to diluting TNF antibodies. One skilled in the art cannot discern where the product is produced which results in a treatment which is different from placebo. One skilled in the art cannot discern where the product produced is "homeopathically potentized form" and mere dilution of an

product because the state of the art only observe placebo effect with such "homeopathically potentized form" of the product.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 3 and 5-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Le et al. (US 5,698,195).

Le et al. disclose anti-TNF antibodies used for treatment of rheumatoid anthritis (columns 34-38). Le et al. teach numerous method of therapeutic administration with different dosages (column 36).

The term "homeopathically potentized antibodies" is not defined and thus the antibodies of Le et al. inherently comprises such properties. The homeopathic dilution terms are relative terms whose metes and bounds cannot be determined since the original concentration prior to dilution is not known. Thus, the dilution term is met by the concentration disclosed by Le et al. In cases where the dilution does not contain the antibody, the undiluted solutions of Le et al. anticipates the claim limitation.

Applicants argue that Le et al. does not teach the claimed homeopathically methodology. However, the it is not clear what is the metes and bounds of the term

which excludes the teachings of Le et al. Furthermore, the treatment of Le et al. uses the same compounds.

Applicants argue that a finding of inherent anticipation requires a showing that while not disclosed explicitly the prior art composition possesss the properties of the claimed composition. However, Le et al. uses the same antibody as the applicant and provides different dosages which are dilutions. Furthermore, if the homeopathically potentized form does not contain the antibody because such low dilutions then the buffer is diclosed by Le et al. If the products are identical the product inherently has the activity claimed.

Applicants argue that the data set forth in the Example 2 of the specification show that the properties of the claimed "homeopathically activated" form of antibodies are different from the placebo control because example 2 was done in the rat model which cannot exhibit placebo effect. However, applicant has not provided evidence that rat model cannot exhibit placebo effect. Furthermore, the sample of example 2 contain more than just the antibody and as such it is not clear which compound is affecting the model. Finally the claims are not limited to a rat model and encompass generically to all "subject".

No evidence is provided that Le et al. compound is not homeopathically potentized form. If the claimed material comprises the antibody then the Le et al. reference provides the antibody. If the claimed material does not comprise the antibody then the Le et al. reference provides the buffer without antibody.

Applicants argue that a prima facie case has not been made for inherency. However, the claimed compound starting material is the same as the antibody of Le et al. The subsequent dilution is taught by Le et al. The dilutions without antibody because of the claim limitation to extreme dilutions is met by the product by process limitation where the non-antibody containing solutions of Le et al.

7. No claims are allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Pak whose telephone number is 571-272-0879. The examiner can normally be reached on 8:00 - 2:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael Pak/
Primary Examiner, Art Unit 1646